REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following remarks.

Status of the Claims

Claims 18-24 and 26-33 are pending in the present application upon entry of the amendment of claims made herein. Claims 2, 3, 6-9 and 11-17 have been cancelled as being drawn to non-elected subject matter. Claim 25 has been cancelled, without prejudice or disclaimer. The cancellation of claims made herein does not constitute acquiescence in the propriety of any objection or rejection made by the examiner, but is made merely to advance the case towards allowance. Applicants, of course, reserve the right to file divisional applications for the non-elected subject matter. Claims 18, 22 and 23 have been amended to define the claimed invention more clearly, keeping in mind the examiner's concerns presented in the objections or rejections. Claims 26 and 27 have been amended to properly depend from claim 23. Claims 28-33 have been added. Support for the new claims can be found throughout the specification, for example, at page 3, line 33 to page 4, line 13 and original claims 2, 3, 6 and 18.

Priority

The examiner has requested applicants to submit a certified copy of the PO0893 application to perfect the claim for foreign priority. Applicants would like to point out that the present application is the U.S. national phase of PCT Application No. PCT/AU97/00436 and thus applicants are not required to submit a certified copy of the priority document to the USPTO as long as applicants met the requirement under PCT Rule 17. Submission of the priority documents during the international stage and the receipt of the priority document by the USPTO are clearly evidenced by the Notification of Acceptance of Application under 35 U.S.C. 371 and 37 CFR 1.494 or 1.495, mailed May 28, 1999. A copy of the notification is attached for the examiner's convenience.

Claim Objections

The examiner has objected to claims 18 and 25 as drawn to a non-elected invention and reciting non-elected species of biological activity. The examiner has further objected to claims 22-23 and 25 as being in improper dependent form for failing to further limit the subject matter of a previous claim. More specifically, the examiner alleges that claims 22 and 23 do not further limit claim 18 because the methods of administration are not clearly altered in any way. With respect to claim 25, the examiner asserts that claim 25 does not further limit the recitation of claim 18 as no disease or condition is specified and thus no further limitation as to the administration of the compound can be discerned. Applicants respectfully traverse these objections.

With respect to the objection to claim 18, applicants understand that finding a generic claim, claim 18, non-allowable, the examiner requests applicants to restrict claim 18 to the elected species, "modifying learning and facilitating memory retrieval." However, as discussed below, applicants believe that claim amended 18, which is generic to biological activities recited therein, is allowable over the prior art references cited in the Office Action. Applicants are entitled to consideration of claims to additional species upon allowance of claim 18. Therefore, applicants respectfully request withdrawal of this objection upon finding claim 18 allowable over the prior art.

Claims 22 and 23 have been amended to properly depend from claim 18 by further limiting claim 18. More specifically, claims 22 and 23 further limit a mammal and administration of a peptide, respectively, which have sufficient antecedent basis in claim 18. In this regard, a disease or condition is sufficiently defined in the amended claims 22 and 23 by referring to its association with abnormality in the biological activity recited in claim 18, which is mediated by abnormality of the neuronal activity. Furthermore, because amended claims 22 and 23 have a linking unity, "said biological activity," with claim 18 applicants believe that these claims are entitled to be considered in the instant application, together with claim 18. Similarly, a new claim 28 that depends from claim 23 and further

limits claim 23 to a specific disease or condition, should be examined together with claim 18, to the extent that claims 18, 23 and 28 are now linked by "said biological activity."

In view of the foregoing, applicants respectfully request reconsideration and withdrawal of all objections.

Claim Rejection

I. Rejection based on 35 USC §112, second paragraph

The examiner has rejected claims 18-24 under 35 USC §112, second paragraph as allegedly indefinite. Specifically, the examiner has objected to the recitation of "an effective amount for modulating neuronal activity" because "such recitation is circular and fails to delineate any specific neuronal activity which is to be effected, amount which is sufficient or test for ascertaining such." Applicants respectfully traverse this rejection.

At the outset, applicants wish to draw the examiner's attention to the amended claim 18, which is now directed to a method of modulating a biological activity and reads "in an effective amount for modulating neuronal activity that mediates said biological activity."

The present specification clearly identifies a number of neuronal activities which mediate biological activities recited in claim 18, upon administration of the peptides of the invention. The peptides of the claimed invention, for example, act as agonists at the AT4 receptor and are therefore involved in motor function, sensory function, and cholinergic function, including cognition. See page 13, lines 6 to 14 of the specification. Moreover, specific experimental paradigms for assessing the cognitive function of the peptides are provided in Examples 11 and 12. Example 13 further describes a method for assessing the effect of the peptides on acetylcholine release in the hippocampus. Given the information provided in the specification, the person skilled in the art will readily be able to determine the range of amounts which is effective for the claimed method.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

II. Rejection based on 35 USC § 102(b) or § 102(e)

The examiner has rejected claims 18-23 under 35 USC § 102(a) or 102(e) as anticipated by US Patent No. 5,599,907 to Anderson *et al.* ("Anderson") or US Patent 5,861,483 to Wolpe *et al.* ("Wolpe"). Applicants respectfully traverse the rejection.

The examiner's rationale in this rejection appears to be based on the claim interpretation that claims 18-23 are simply directed to administration of the recited peptides because "the effective amounts or dosages cannot be discerned as claimed." With this claim interpretation, the examiner alleges that the recited properties are inherently encompassed by Anderson or Wolpe.

As previously stated, claim 18 has been amended to be directed to a method of modulating "a biological activity," which is more precisely specified in the body of claim 18. Furthermore, "an effective amount" of a neuroactive peptide to be administered in the claimed method is more clearly defined by referring to the fact that neuronal activity mediates the biological activity. In view of the amendment of claim 18, applicants respectfully submit that claims 18-24, as well as new claims 28-31, should be interpreted as a method of modulating biological activities recited in claim 18.

Neither Anderson nor Wolpe teach or suggest that peptides disclosed therein can modulate a biological activity recited in claim 18.

Anderson relates to an intact, multimeric haemoglobin-like protein which is useful for supplementing the oxygen carrying capacity of blood as a blood substitute.

Wolpe discloses a number of different hemoglobin peptides. These are mostly from the alpha chain of hemoglobin, whereas the sequence set out in claim 18 is from the beta chain. Wolpe refers only to use of hemoglobin peptides to inhibit proliferation of haematopoietic stem cells, as assessed using an in vivo stem cell

proliferation inhibition assay. There is absolutely no disclosure or suggestion that any of the peptides referred to in Wolpe could act on any neural stem cells.

To make up for the lack of disclosure, the Examiner seems to rely on an inherency theory. Contrary to the examiner's allegation, however, neither supplementing oxygen carrying capacity nor inhibiting stem cell proliferation qualifies as inherent disclosure of the specific biological activities recited in the amended claim 18. Supplementing oxygen carrying capacity is based on a general property of hemoglobin-like proteins carrying oxygen. Cell division characteristics of cells associated with modulation of neuronal activity are known to be very different from that of the highly proliferative nature of the stem cells disclosed in Wolpe. Indeed, stem cells referred to in Wolpe are undifferentiated cells whereas the cells that modulate neuronal activity are differentiated cells. Since neural stem cells are of completely different lineage from haematopoietic stem cells, the person skilled in the art would have no expectation that a peptide which acts on a haematopoietic stem cell would also act on a neural stem cell.

Thus, a person of ordinary skill would not recognize that peptides for supplementing oxygen carrying capacity or inhibiting stem cell proliferation could modulate biological activities as recited in claim 18.

In relying upon the theory of inherency the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). Applicants respectfully submit that the examiner fails to meet such burden in this case. The Examiner has not provide any basis or technical reasoning how modulating the specified biological activities of the recited neuroactive peptide necessarily flows from the teachings of Anderson or Wolpe that their peptide can be used to supplement oxygen carrying capacity of blood or to inhibit stem cell proliferation. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534 (Fed. Cir.

1993). Also, inherency may not be established by probabilities or possibilities. *In re Robertson,* 169 F.3d 743, 745 (Fed. Cir. 1999).

Thus, given the lack of disclosure in Anderson or Wolpe, combined with the absence of any other objective evidence curing the missing description, a person of ordinary skill in the art would not infer from Anderson or Wolpe that the ability to modulate the specific biological activities recited in claim 18 is an inherent property of any of the peptides disclosed in the prior art references.

It is axiomatic that, for a reference to be anticipatory, it must describe each and every element of the claimed invention. However, neither Anderson nor Wolpe, explicitly or inherently, teaches modulation of any one of the biological activities recited in claim 18. Accordingly, none of the cited references discloses each and every element of the claimed invention either explicitly or inherently.

Accordingly, reconsideration and withdrawal of all of the anticipation rejections are respectfully requested.

III. Rejection based on 35 U.S.C. §103(a)

The examiner has rejected claim 24 as obvious over Anderson in view of Kandel et al. ("Kandel") and Relton et al. ("Relton"). The examiner has further rejected claim 24 over Wolpe in view of Kandel and Wilkinson et al. ("Wilkinson"). Applicants respectfully traverse this rejection.

As set forth above, none of the primary references, Anderson or Wolpe, disclose or suggest a method of modulating a biological activity as recited in amended claim 18 by using the peptide disclosed therein.

Kandel provides a general disclosure regarding the prominence of the blood-brain barrier in restricting peptides and other larger molecules from entering the brain and CNS. Relton discloses intracerebroventricular injection of Lipocortin-1 that is a peptide useful for inhibiting the inflammatory injury associated with ischemia. Wilkinson teaches intracerebral injection of methotrexate for the treatment of rat gliosarcoma brain tumors.

Thus, none of these secondary references teaches a method of modulating a biological activity as recited in claim 18 using the recited neuroactive peptide. Accordingly, the cited references, alone or in combination, fail to teach or suggest the claimed invention.

In conclusion, there exists no *prima facie* case of obviousness, and therefore reconsideration and withdrawal of the rejection are respectfully requested.

In view of the foregoing amendments and remarks, applicants respectfully request favorable reconsideration and allowance of the pending claims. If there are any issues remaining which the examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the examiner is hereby respectfully invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Date: March 19, 2002

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Marker-Up Version

18. (Amended) A method of modulating **a biological activity** [neuronal activity], comprising administering to a mammal a neuroactive peptide in an amount effective for modulating neuronal activity **that mediates said biological activity** [in need thereof], wherein said neuroactive peptide comprises the amino acid sequence:

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe, (SEQ ID NO:1),

and wherein said [neuroactive peptide modulates at least one] biological activity **is** selected from the group consisting of modifying learning, modifying behaviour, [vasocative effects, dilation of cerebral arteries, increase in renal blood flow,] increase in sterotypic behaviour, facilitating memory retrieval, neurite modeling and alleviation of the effects of spinal cord injury.

22. (Amended) The method of claim 18, [which is a prophylactic method] **wherein said mammal is at risk of developing a disease or condition associated with abnormality in said biological activity, said abnormality being mediated by abnormality of said neuronal activity**.

23. (Amended) The method of claim 18, [which is a therapeutic method] **wherein said peptide is administered in an amount effective for treating a disease or condition associated with abnormality in said biological activity, said abnormality being mediated by abnormality of said neuronal activity**.

26. (Amended) The method of claim [25] **23**, wherein the peptide is administered by inhalation.

27. (Amended) The method of claim [25] **23**, wherein the peptide is administered intracerebrally.